

# TOWAR: Type O Whole Blood and Assessment of Age During Prehospital Resuscitation

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Military Health System Research Symposium

- **Francis Guyette MD, MPH – W81XWH2210610 Rapid Assessment for Prehospital Triage of Evacuation and medical Resources en ROute Care Award (RAPTER ERCA) and HR00112320015 Sensor observed Treatment, Annotation and Timing (STAT)**
- **Jason Sperry MD, MPH - No conflicts to report**
- **Stephen Wisnieski PhD - No conflicts to report**
- **The views and conclusions contained herein are those of the author(s) and should not be interpreted as representing the official policies or endorsements, either expressed or implied, of the U.S. Government.**

# Objectives

- To review the key observations regarding early resuscitation with blood
- To describe the TOWAR study and its findings
- To discuss the implications of the TOWAR study for early resuscitation

# In-Hospital Whole Blood Resuscitation

Research

JAMA Surgery | Original Investigation

## Association of Whole Blood With Survival Among Patients Presenting With Severe Hemorrhage in US and Canadian Adult Civilian Trauma Centers

Crisanto M. Torres, MD, MPH; Alistair Kent, MD, MPH; Dane Scantling, D;  
Elliott R. Haut, MD, PhD; Joseph V. Sakran, MD, MPH, MPA

ASA PAPER

## Whole Blood is Superior to Component Transfusion for Injured Children

*A Propensity Matched Analysis*

Christine M.

SOUTHERN SURGICAL ASSOCIATION ARTICLES

## Impact of Incorporating Whole Blood into Hemorrhagic Shock Resuscitation: Analysis of 1,377 Consecutive Trauma Patients Receiving Emergency-Release Uncrossmatched Blood Products

Jason B Brill, MD, Brian Tang, BS, Gabrielle Hatton, MD, Krislynn M Mueck, MD,  
C Cameron McCoy, MD, Lillian S Kao,

ASA PAPER

## Use of Cold-Stored Whole Blood is Associated With Improved Mortality in Hemostatic Resuscitation of Major Bleeding

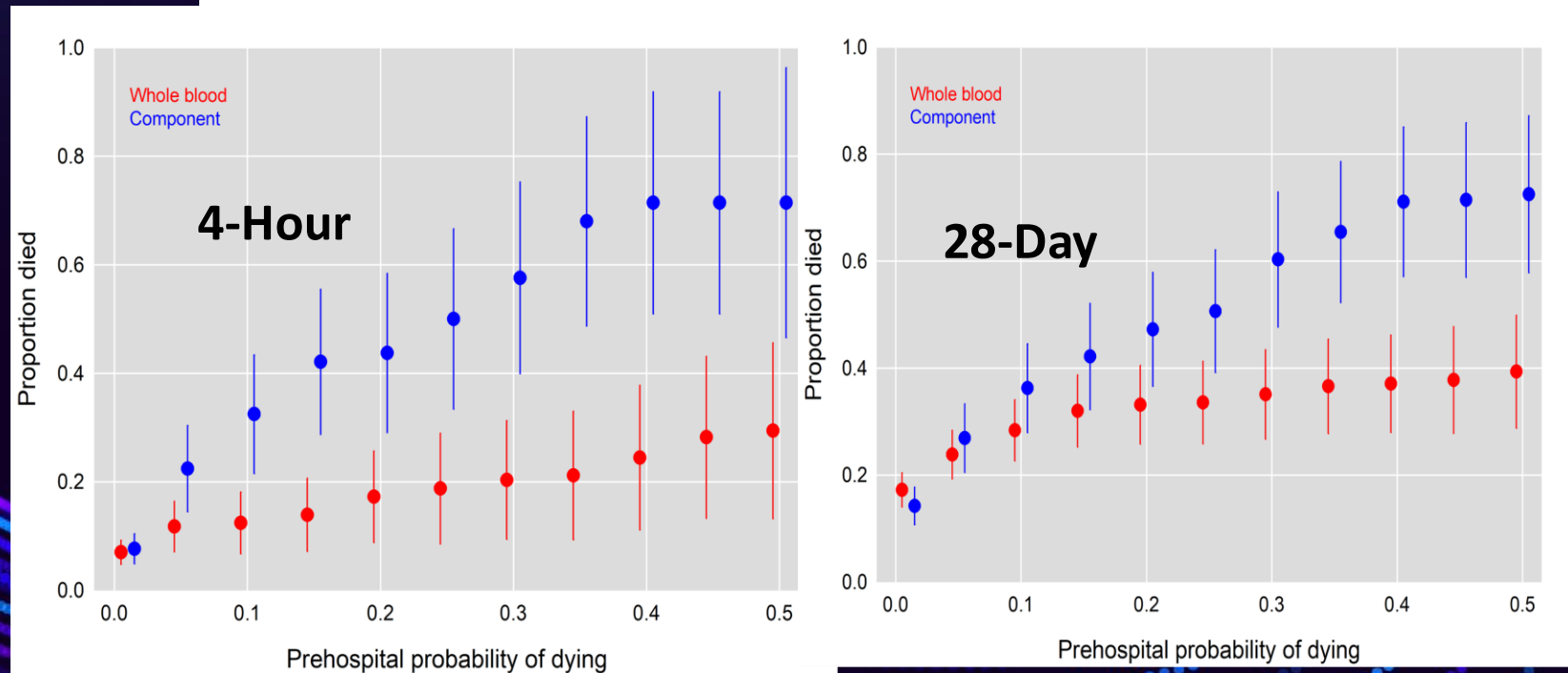
*A Multicenter Study*

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James E. Babowice, DO,¶¶ Charles Mains, MD,## Robert M. Madaya, MD,##  
Haytham M.A. Kaafarani, MD, MPH,\*\*\* Ava K. Mokhtari, MD,\*\*\*  
Sarah A. Moore, MD,††† Kathleen Madden, MD,††† Allen Tanner, II, MD,‡‡‡  
Diane Redmond, MSN,‡‡‡ David J. Millia, MD,§§§ Amber Brandolino, MS,§§§  
Uyen Nguyen, BS,||||| Fernon Churchill, PhD,¶¶¶ Scott B. Armen, MD,###  
and John M. Porter, MD,\*\*\*\*

# TO 0002: Primary Analysis

## Whole Blood Resuscitation and Association with Survival in Injured Patients with an Elevated Probability of Mortality

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ORIGINAL ARTICLE

## Prehospital Resuscitation with Type O Whole Blood for Trauma and Hemorrhage

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# TOWAR Trial

Type O Whole Blood and Assessment of Age During Prehospital Resuscitation

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**TOWAR:** Phase III, 4 Year, Multicenter, Prospective, Randomized, Open-label, Interventional Trial

**Exception From Informed Consent:** FDA IND Approved

- Investigational New Drug 26968

# TOWAR Trial

To determine if prehospital whole blood improves outcomes compared to component blood resuscitation in patient with hemorrhagic shock

10 participating trauma centers – U.S. and Canada

Primary Outcome: 30-day mortality

Secondary Outcomes: Mortality 3,6,24-hour,

Death due to exsanguination, Death due to brain injury,

Blood transfusion requirements (24hr), Achievement of hemostasis, organ failure,

Nosocomial infection, Acute Respiratory Distress Syndrome, Coagulation measurements

Prespecified Observational Sub-Study:

Age of Whole Blood: 1-14 days vs. 15-21 days

# TOWAR Trial

## Pragmatic Inclusion Criteria

1. Injured patients at risk of hemorrhagic shock being transported from scene or referral hospital to a participating TOWAR trial site that meet requirements for initiation of blood or blood components.

AND

- 2A. Systolic blood pressure  $\leq 90$ mmHg and Tachycardia (HR  $\geq 108$ ) at scene, at outside hospital or during transport.

OR

- 2B. Systolic blood pressure  $\leq 70$ mmHg at scene, at outside hospital or during transport.

# TOWAR Trial

## Randomization

**Cluster Randomization Scheme – Air medical service/base**

**2/3 Whole Blood and 1/3 Component Blood**

**Randomly assigned to one of 3 repeated sequences**

**WB, WB, Component  
WB, Component, WB  
Component, WB, WB**

*Selected to minimize blood waste, simplify delivery logistics and ensure adequate power for the whole blood observational sub-study*

# TOWAR Trial

## Intervention / Comparison Arms

### OPEN LABEL

#### Whole Blood Group

Up to 2 units cold stored Low Titer Type O + Whole Blood (Anti-A and anti-B titers  $< 256$ )

Out to 21 days

Utilize existing practice if in place

### Versus

#### Component Blood Group

Red cell and/or Plasma Component prehospital resuscitation

Standard site resuscitation utilizing existing practice if in place

*No other aspect of clinical care prehospital or in-hospital were modified*

# TOWAR Trial

## Analysis Plan

30-day Mortality: Groups compared using a two-sided Donner–Klar test for proportions.

A mixed-effects logistic regression model was used to estimate the association between whole blood and 30-day mortality

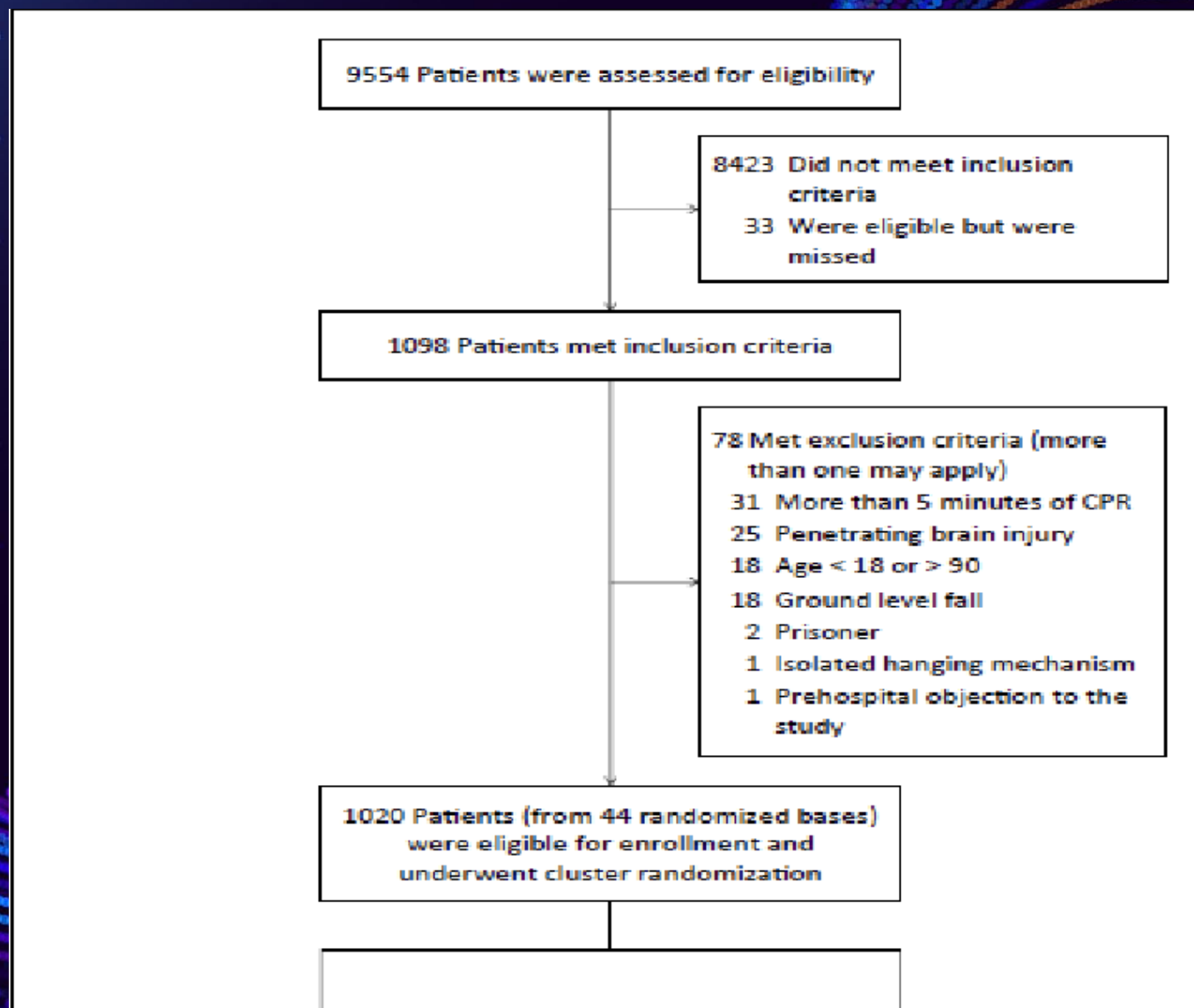
Age of Whole Blood Sub-study: A generalized boosted regression model was used to estimate propensity scores for receipt of older whole blood (15–21 days)

# TOWAR Trial

## Prespecified Subgroups

- 1) Patients with and without significant traumatic brain injury (Head abbreviated injury scale- AIS >2)
- 2) Patients arrived from the scene of injury versus referral hospital
- 3) Patients who had severe prehospital hypotension (SBP <70mmHg)
- 4) Age (55 yo dichotomized)
- 5) Sex
- 6) Race
- 7) Trauma center / Site

# Enrollment



# TOWAR Trial: Cohort Comparison

Table 1. Characteristics of the Enrolled Patients

| Characteristic                               | Whole Blood<br>(N = 715) | Component Blood<br>(N = 305) |        |
|----------------------------------------------|--------------------------|------------------------------|--------|
| Mean age — yr                                | 44.8±18.9                | 45.5±19.3                    |        |
| Female sex — no. (%)                         | 193 (27.3)               | 77 (25.3)                    |        |
| Non-white race — no. (%)                     | 168 (26.6)               | 80 (27.7)                    |        |
| Hispanic ethnicity — no. (%)                 | 65 (10.6)                | 31 (11.8)                    |        |
| Injury type — no. (%)                        |                          |                              |        |
| Blunt                                        | 564 (79.8)               | 233 (76.4)                   |        |
| Penetrating                                  | 143 (20.2)               | 72 (23.6)                    |        |
| Abbreviated Injury Scale — no. (%)‡          |                          |                              |        |
| Head/Neck >2                                 | 260 (39.3)               | 106 (36.6)                   |        |
| Face >2                                      | 26 (3.9)                 | 16 (5.5)                     |        |
| Chest >2                                     | 386 (58.4)               | 155 (53.4)                   |        |
| Abdomen >2                                   | 222 (33.6)               | 112 (38.6)                   |        |
| Extremity >2                                 | 268 (40.5)               | 120 (41.4)                   |        |
| External >2                                  | 11 (1.7)                 | 3 (1.0)                      |        |
| Injury Severity Score — median (IQR)§        | 25.0 (16.0–34.0)         | 23.0 (14.0–34.0)             |        |
| Qualifying Glasgow Coma Scale — median (IQR) | 11.0 (3.0–15.0)          | 13.0 (3.0–15.0)              |        |
| <u>Traumatic brain injury — no. (%)</u>      | <u>296 (41.4)</u>        | <u>109 (35.7)</u>            |        |
| Transferred from — no. (%)                   |                          |                              |        |
| Scene of injury                              | 507 (70.9)               | 215 (70.5)                   | P=0.09 |
| Other hospital                               | 208 (29.1)               | 90 (29.5)                    |        |
| Prehospital interventions — no. (%)          |                          |                              |        |
| <u>Intubation</u>                            | <u>389 (54.4)</u>        | <u>147 (48.4)</u>            |        |
| CPR                                          | 74 (10.4)                | 22 (7.3)                     |        |
| Defibrillation                               | 12 (1.7)                 | 3 (1.0)                      | P=0.08 |
| Tourniquet                                   | 94 (13.1)                | 49 (16.1)                    |        |
| Pelvic binder                                | 155 (21.7)               | 67 (22.0)                    |        |
| Tranexamic acid                              | 298 (41.8)               | 114 (37.5)                   |        |
| Crystalloids/colloids                        | 446 (62.6)               | 192 (63.4)                   |        |

# TOWAR Trial

## Primary Outcome 30-day mortality

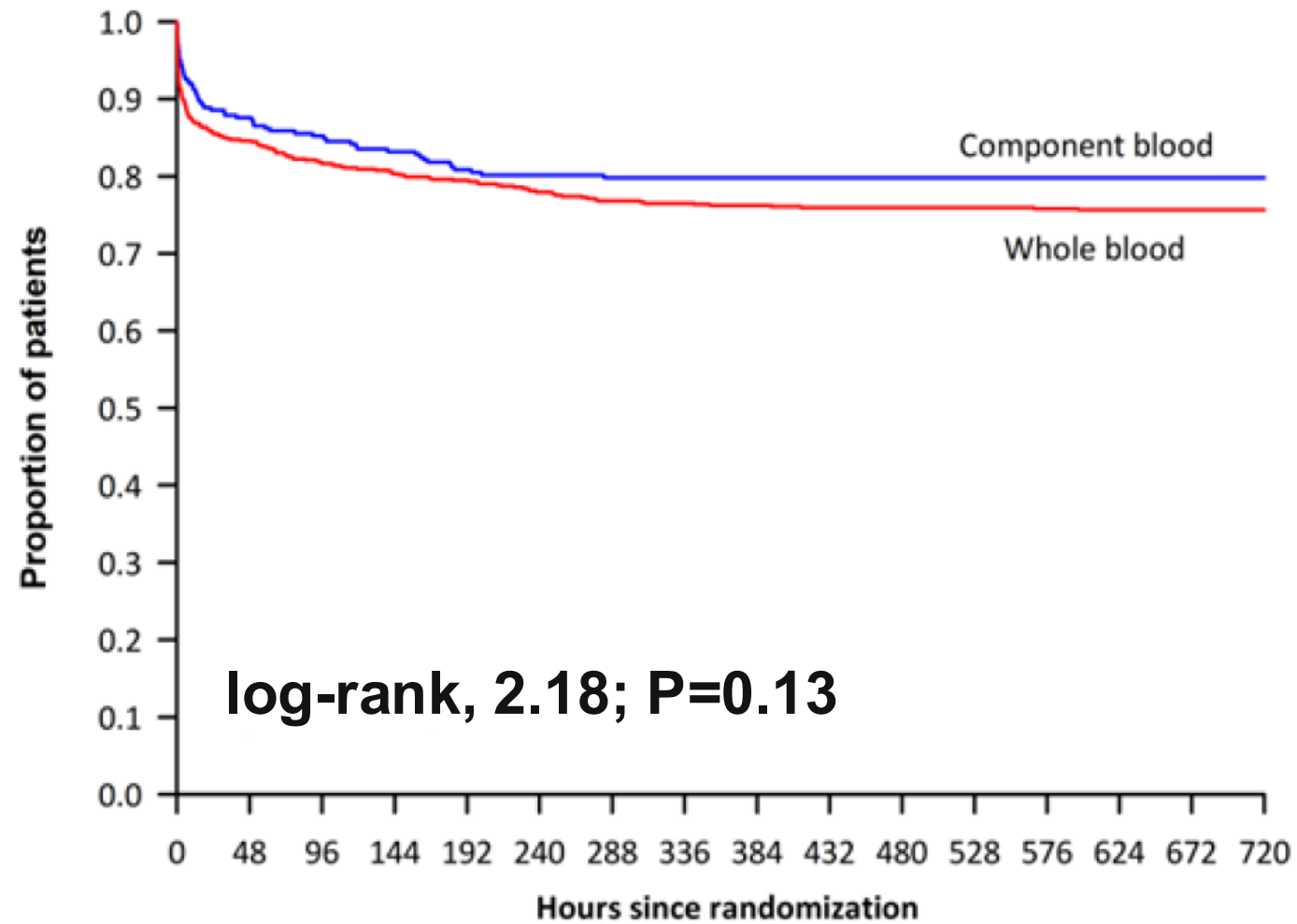
Whole Blood Group vs. Component Blood Group  
(N=695) (N=298)

180 (25.9%)

61 (20.5%)

Adjusted OR 1.24  
95% CI, 0.87–1.76  
P=0.24

# Kaplan-Meier 30-day Mortality

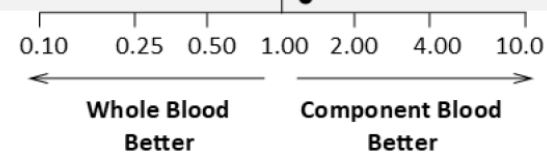


## No. at Risk

|                 |     |     |     |     |     |     |     |
|-----------------|-----|-----|-----|-----|-----|-----|-----|
| Whole blood     | 681 | 552 | 532 | 520 | 518 | 516 | 516 |
| Component blood | 297 | 249 | 239 | 238 | 237 | 237 | 237 |

# B 30-Day Mortality in Prespecified Subgroups

| Subgroup                              | No. of Patients | Whole Blood<br>no. of events/total no. (%) | Component Blood<br>no. of events/total no. (%) | Odds Ratio (95% CI) |
|---------------------------------------|-----------------|--------------------------------------------|------------------------------------------------|---------------------|
| Head or neck AIS score >2             |                 |                                            |                                                |                     |
| Yes                                   | 359             | 81/254 (31.9)                              | 35/105 (33.3)                                  | 0.92 (0.55–1.54)    |
| No                                    | 566             | 70/388 (18.0)                              | 25/178 (14.0)                                  | 1.20 (0.71–2.04)    |
| Transferred from                      |                 |                                            |                                                |                     |
| Scene of injury                       | 703             | 133/491 (27.1)                             | 47/212 (22.2)                                  | 1.26 (0.84–1.89)    |
| Other hospital                        | 290             | 47/204 (23.0)                              | 14/86 (16.3)                                   | 1.21 (0.60–2.46)    |
| Severe hypotension ( $\leq 70$ mm Hg) |                 |                                            |                                                |                     |
| Yes                                   | 543             | 130/377 (34.5)                             | 40/166 (24.1)                                  | 1.59 (1.02–2.47)    |
| No                                    | 450             | 50/318 (15.7)                              | 21/132 (15.9)                                  | 0.84 (0.47–1.51)    |
| Age, yr                               |                 |                                            |                                                |                     |
| 18–55                                 | 679             | 90/481 (18.7)                              | 25/198 (12.6)                                  | 1.50 (0.86–2.61)    |
| $\geq 56$                             | 307             | 85/209 (40.7)                              | 35/98 (35.7)                                   | 1.31 (0.78–2.17)    |
| Sex                                   |                 |                                            |                                                |                     |
| Male                                  | 720             | 130/498 (26.1)                             | 46/222 (20.7)                                  | 1.23 (0.82–1.86)    |
| Female                                | 263             | 46/188 (24.5)                              | 15/75 (20.0)                                   | 1.11 (0.54–2.26)    |
| Race                                  |                 |                                            |                                                |                     |
| White                                 | 654             | 117/450 (26.0)                             | 43/204 (21.1)                                  | 1.28 (0.84–1.95)    |
| Non-White                             | 244             | 29/165 (17.6)                              | 13/79 (16.5)                                   | 0.79 (0.37–1.68)    |
| Study site                            |                 |                                            |                                                |                     |
| A                                     | 150             | 27/107 (25.2)                              | 6/43 (14.0)                                    | 1.91 (0.68–5.31)    |
| B                                     | 248             | 35/155 (22.6)                              | 17/93 (18.3)                                   | 1.05 (0.52–2.10)    |
| C                                     | 68              | 16/44 (36.4)                               | 7/24 (29.2)                                    | 1.22 (0.38–3.95)    |
| D/E/K                                 | 64              | 11/54 (20.4)                               | 4/10 (40.0)                                    | 0.40 (0.09–1.89)    |
| F                                     | 39              | 7/30 (23.3)                                | 3/9 (33.3)                                     | 1.04 (0.18–5.96)    |
| G                                     | 116             | 19/88 (21.6)                               | 4/28 (14.3)                                    | 1.50 (0.45–5.00)    |
| H                                     | 62              | 14/42 (33.3)                               | 4/20 (20.0)                                    | 2.15 (0.55–8.37)    |
| I                                     | 113             | 32/85 (37.6)                               | 6/28 (21.4)                                    | 2.33 (0.78–6.91)    |
| J                                     | 133             | 19/90 (21.1)                               | 10/43 (23.3)                                   | 0.77 (0.31–1.91)    |
| Overall                               | 992             | 180/695 (25.9)                             | 61/297 (20.5)                                  | 1.24 (0.87–1.76)    |



| Secondary Outcome                               | Whole Blood<br>(N = 695) | Component Blood<br>(N = 298) | Effect Estimate<br>OR / HR / IRR / $\beta$<br>(95% CI) |
|-------------------------------------------------|--------------------------|------------------------------|--------------------------------------------------------|
| 3-hour mortality — no. (%)                      | 64 (9.4)                 | 16 (5.4)                     | 1.72 (0.96 to 3.08)                                    |
| 6-hour mortality — no. (%)                      | 76 (11.2)                | 21 (7.0)                     | 1.55 (0.92 to 2.62)                                    |
| 24-hour mortality — no. (%)                     | 98 (14.4)                | 33 (11.1)                    | 1.25 (0.81 to 1.93)                                    |
| In-hospital mortality — no. (%)                 | 171 (24.8)               | 58 (19.5)                    | 1.25 (0.87 to 1.78)                                    |
| Death by exsanguination — no. (%)               | 61 (9.0)                 | 23 (7.8)                     | 1.08 (0.65 to 1.81)                                    |
| Death by TBI or herniation — no. (%)            | 61 (9.0)                 | 23 (7.8)                     | 0.98 (0.56 to 1.71)                                    |
| Units transfused 24 h of arrival — median (IQR) |                          |                              |                                                        |
| Whole                                           | 0.0 (0.0–1.0)            | 0.0 (0.0–1.0)                | 0.91 (0.69 to 1.21)                                    |
| Plasma                                          | 1.0 (0.0–4.0)            | 1.0 (0.0–5.0)                | 0.85 (0.66 to 1.11)                                    |
| Platelets                                       | 0.0 (0.0–1.0)            | 0.0 (0.0–1.0)                | 0.86 (0.63 to 1.17)                                    |
| Red cells                                       | 1.0 (0.0–4.0)            | 2.0 (0.0–5.0)                | 0.86 (0.67 to 1.09)                                    |
| Cryoprecipitate                                 | 0.0 (0.0–0.0)            | 0.0 (0.0–0.0)                | 0.81 (0.49 to 1.32)                                    |
| Hemostasis — no. (%)‡                           | 619 (89.2)               | 277 (93.6)                   | 0.61 (0.35 to 1.04)                                    |
| Minutes to achievement — median (IQR)           | 60.0 (60.0–78.0)         | 60.0 (60.0–80.0)             | 0.98 (0.88 to 1.09)                                    |
| Multiple organ failure — no. (%)§               | 98 (14.1)                | 37 (12.4)                    | 1.12 (0.74 to 1.69)                                    |
| Nosocomial infection — no. (%)                  | 57 (8.2)                 | 26 (8.7)                     | 0.92 (0.55 to 1.54)                                    |
| Acute respiratory distress syndrome — no. (%)   | 273 (39.3)               | 121 (40.6)                   | 0.87 (0.66 to 1.17)                                    |
| INR >1.5 within 1 h of arrival — no. (%)        | 109 (20.3)               | 57 (26.4)                    | 0.69 (0.46 to 1.02)                                    |
| PT within 1 h of arrival — median (IQR)         | 14.2 (12.3–16.4)         | 14.5 (12.2–16.5)             | 0.05 (-0.68 to 0.78)                                   |

**Table S10: Safety and Adverse Event Comparison Across Intent-To-Treat Groups**

| <b>Variable</b>                          | <b>Whole<br/>Blood<br/>(N = 715)</b> | <b>Component<br/>Blood<br/>(N = 305)</b> |
|------------------------------------------|--------------------------------------|------------------------------------------|
| No. of patients who had an adverse event | 3                                    | 1                                        |
| No. of adverse events                    | 4                                    | 1                                        |
| Acute respiratory distress syndrome      | 1†                                   | 0                                        |
| Transfusion reaction                     | 1†                                   | 1                                        |
| Transfusion-related acute lung injury    | 1†                                   | 0                                        |
| Creatinine >1.5 mg/dL within 24 h        | 1                                    | 0                                        |

\* Restricted to possibly related events.

† Serious adverse event.

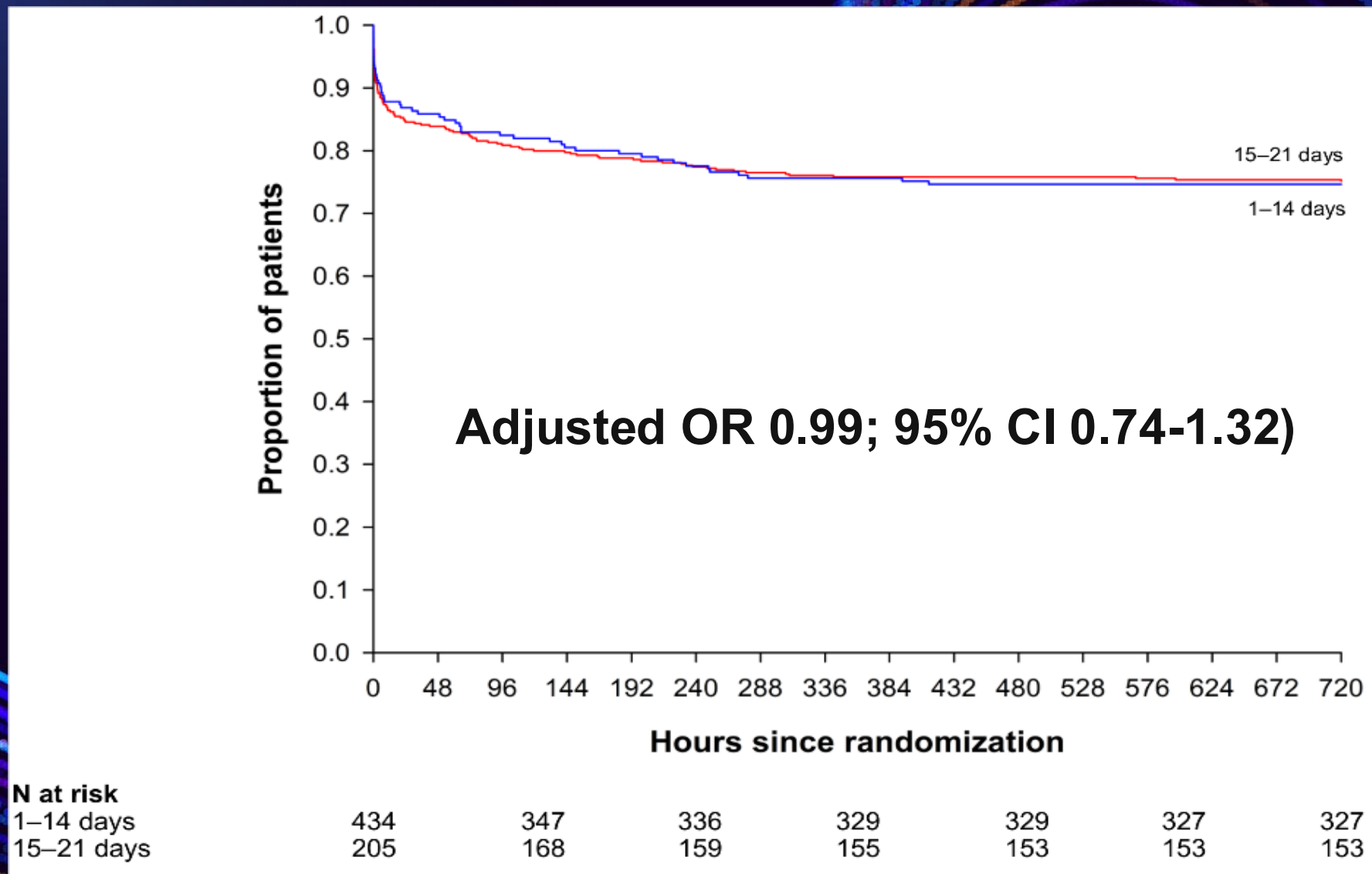
# Procedures

**Table S20: Surgical Procedures Across Intent-to-Treat Groups\***

| <b>Surgical Procedure — no. (%)</b>                      | <b>Whole Blood<br/>(n=695)</b> | <b>Component Blood<br/>(n=298)</b> |
|----------------------------------------------------------|--------------------------------|------------------------------------|
| No. surgical procedures                                  |                                |                                    |
| Thoracotomy/Sternotomy                                   | 29 (6.1)                       | 19 (8.6)                           |
| Exploratory Laparotomy                                   | 223 (46.8)                     | 108 (48.9)                         |
| Craniotomy/Craniectomy                                   | 14 (2.9)                       | 7 (3.2)                            |
| Interventional Radiology/Embolization                    | 63 (13.2)                      | 30 (13.6)                          |
| Orthopedic                                               | 95 (20.0)                      | 53 (24.0)                          |
| Resuscitative Endovascular Balloon Occlusion<br>of Aorta | 10 (2.1)                       | 1 (0.5)                            |
| Laparoscopy                                              | 6 (1.3)                        | 2 (0.9)                            |
| Chest Tube/Thoracostomy                                  | 60 (12.6)                      | 29 (13.1)                          |
| Other                                                    | 236 (49.6)                     | 108 (48.9)                         |

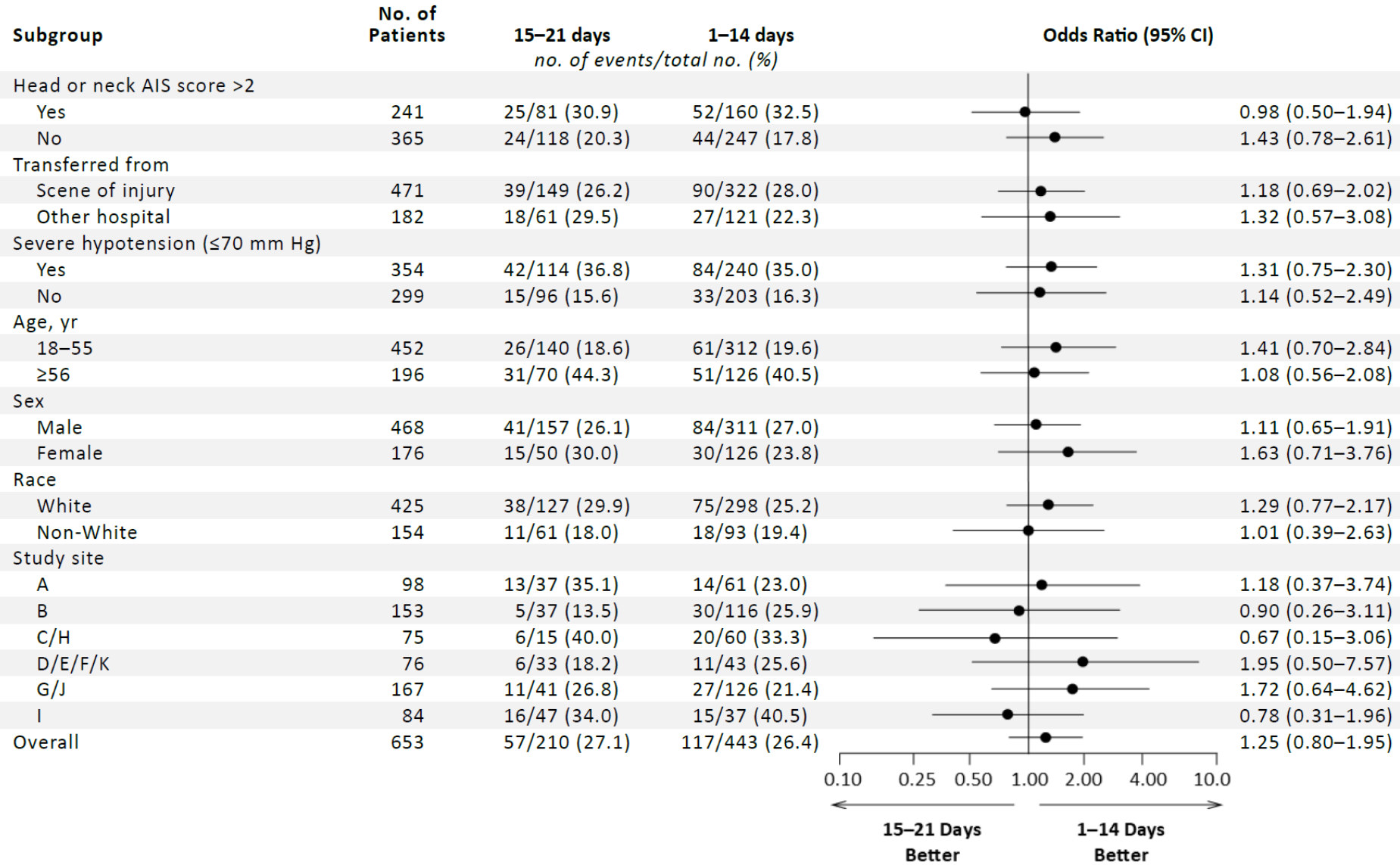
\* No statistically significant differences were observed between the groups

## Sub-Study: WB Age 1-14 d vs 15-21 d



# Age WB Prespecified Subgroups

**B 30-Day Mortality in Prespecified Subgroups**



# Conclusions

- In injured patients requiring prehospital blood transfusion at risk of hemorrhagic shock, whole blood did not result in a lower 30-day mortality
- The storage age of whole blood through 21 days from donation was not associated with apparent differences in outcomes

# Acknowledgements

## Co-Principal Investigators

- Dr. Jason Sperry
- Dr. Stephen Wisniewski
- Laura Vincent
- Abigail Cotton

## Co-Investigators

- Dr. Joshua Brown
- Dr. Matthew Neal
- Dr. Raquel Forsythe
- Dr. Daryl Triulzi
- Dr. Mark Yazer
- DoW
- MACRO

Thank You!

## LITES Staff

- James Luther



# Evolving Prehospital Care

- 33.0% Mortality – PAMPer Controls
  - Enrolled May 2014- Oct 2017



Resuscitation  
TXA  
TBI guidelines  
???

- 24.3% Mortality- All patients TOWAR
  - Enrolled May 2022- June 2025